

### **Remarks**

Prior to entry of the Amendment Claims 1 - 29 were pending in the present application. Claims 26 – 28 are allowed. With this amendment, Claims 6 and 7 are canceled. Claim 29 is amended to be an independent claim rather than depending on Claim 28. Claims 30 - 31 are newly added. Support for the amendments and new claims is found in the specification as originally filed, see for example paragraph 66-67, Table 1, and original Claims 6 and 7. Applicants reserve the right to prosecute the originally filed, broader, and/or similar claims in one or more additional applications and do not waive any of their rights or abandon any non-elected subject matter. The amendments and the various rejections raised in the Office Action are discussed in more detail below.

### **Claim Objections**

Claim 29 stands objected to under 37 CFR 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of the previous claim. Applicants have amended Claim 29 to be an independent claim correcting the alleged improper dependency to Claim 28. Accordingly, in light of the amendment, Applicants respectfully request withdrawal of the objection to Claim 29, under 37 CFR 1.75(c).

### **Rejection under 35 C.F.R. §112, second paragraph**

Claims 6 and 7 stand rejected under 35 C.F.R. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. Applicants traverse the rejection.

Claim 6 recites the phrase “hybridizes”, but does not recite conditions under which hybridization must occur. Applicants respectfully submit that hybridizes is well know term in the art. In addition, the specification describes exemplarily hybridization conditions (see for example, specification at paragraphs 67 and 68). Although Applicants must respectfully disagree with the Patent Office argument and rationale, in order to further the prosecution of the present application and Applicants’ business interests, yet without acquiescing to the Examiner’s arguments, Applicants have canceled Claims 6 and 7.

**Rejection under 35 C.F.R. §112 first paragraph: enablement**

Claims 6 and 7 stand rejected under 35 C.F.R. §112, first paragraph as allegedly failing to comply with the enablement requirement. Applicants traverse the rejection.

Applicants submit that the claims satisfy the enablement requirement for the follow reasons. Claim 6, recites a variant *H. jecorina* CBH1 cellulase, wherein said variant comprises a substitution or deletion at a position corresponding to T66 of the mature *H. jecorina* CBH1 protein (SEQ ID NO. 2), wherein said variant *H. jecorina* CBH1 cellulase has cellulolytic activity and the variant is encoded by a nucleic acid sequence that hybridizes to a nucleic acid sequence having about 80% sequence identity to (SEQ ID NO: 1). Dependent Claim 7 is directed to variant *H. jecorina* CBH1 cellulase according to Claim 6, wherein said variant comprises a substitution at a position corresponding to a residue selected from the group consisting of Q186(E), S195(A/F), E239S, G242(H/Y/N/S/T/D/A) and P412(T/S/A). As the specification discloses, Applicants have identified possible sites involved in the stability of the CBH1 enzyme in three different ways based on alignment of the sequences of the homologs with CBH1. In the first method, sites that differed between the *H. jecorina* CBH1 catalytic domain and the catalytic domain of at least one of the homologs of lower stability (*i.e.*, excluding only *H. orientalis*) were identified as possible sites involved in the thermostability of CBH1. The sites identified included, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) in CBH1 from *H. jecorina*. In the second method, sites where the residue in *H. jecorina* or *H. orientalis* is the same as that found in all of the decreased stability enzyme homologs resulted in the identification of sites that lacked correlation with  $T_m$ . Again, the specification describes that the sites identified as retaining relevance with stability included, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) in CBH1 from *H. jecorina*. In the third method described in the specification, sites where *H. jecorina* and *H. orientalis* are the same, with the corresponding residue in *H. schweinitzii* being either the same or different as in either of these two, but a different amino acid in the corresponding site of either *T. konilangbra* or *T. pseudokoningii* were considered as possible sites involved in thermostability of the enzyme. The sites identified included,

*inter alia*, the sites presently claimed in Claim 7 (Q186, S195, and P412) in CBH1 from *Hypocrea jecorina*. Finally, the specification teaches the variant CBH1 polypeptides comprise a substitution or deletion at a position corresponding to one or more of residues, including, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) (See, specification, paragraph [0208]).

Applicants assert that a specification which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of under 35 C.F.R. §1.12 first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. (See, MPEP, Section 2164.04). In addition, Applicants assert that a person of ordinary skill in the art reading Applicants specification at the time it was filed would have been able to make and use the presently claimed invention. This is particular true given the level of skill in the art and the teaching of Applicants' specification. For example, Figure 2 of Applicants specification provides an alignment of 5 CBH1 homologs. The alignment indicates which regions are conserved. As described above, Applicants have identified possible sites involved in the stability of the CBH1 enzyme in three different ways based on alignment of the sequences of the homologs with CBH1. A person of ordinary skill in the art would readily have been able use standard methods to make the cellulases containing the substitutions or deletions at the claimed sites, particularly since the examples of such methods are set forth in Applicants specification.

Finally, the Patent Office maintains that undue experimentation would be required to produce active proteins with the claimed changes. (See, Office Action, page 3). Applicants respectfully remind the Patent Office that compliance with the enablement requirement of 35 U.S.C. 112, first paragraph does not turn on whether an example is disclosed. In fact, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 164 USPQ 642 (CCPA 1970). Because only an enabling disclosure is required, applicant need not describe all actual embodiments. (See, MPEP, Section 2164.02). Although the variants would need to be assayed for activity, the present Specification

provides the means to conduct the assay. (See, Specification, paragraph [0283], and Example 2 paragraphs [0343]-[0344]. Simply requiring additional testing (the methods for which are provided in the Specification itself, does not render the Claims non-enabled. There is indeed an expectation of success, through the use of the assay methods provided in the Specification. Indeed the present specification explicitly teaches the variant CBH1 polypeptides comprise a substitution or deletion at a position corresponding to one or more of residues, including, *inter alia*, the sites presently claimed in Claim 6 (T66) and Claim 7 (Q186, S195, E239, G242, P412) (See, specification, paragraph [0208]) and teaches how to assess the activity of the enzyme.

Applicants respectfully submit that the rejection of Claims 6 and 7, under 35 U.S.C. 112§, first paragraph, enablement be withdrawn, however, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have canceled Claims 6 and 7.

### **Conclusion**

In light of the above amendments, as well as the above remarks, Applicants believe the pending claims are in condition of allowance and issuance of a Notice of Allowance is respectfully requested. If a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (650) 846-7614.

Respectfully submitted,

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